On page 2, lines 2-7 please replace "is a continuation-in-part of application Serial No. 09/127,620, flied August 1, 1998, which is a continuation-in-part of application Serial No. 08/843,157, filed April 11, 1997, now abandoned, which is a continuation in part of application Serial No. 08/581,351, filed December 29, 1995, now U.S. Patent No. 5,767,135, and which claims priority to provisional application Serial No. 60/024,221, filed October 22,1996 and to provisional application Serial No. 60/026,992, filed September 20, 1996" with - - claims priority under 35 U.S.C. §119(e) to provisional patent application serial number 60/182,608, filed February 15, 2000. - -

REMARKS

Claims 13-83 are pending. Claims 13-83 have been rejected. A pending claims sheet and replacement paragraph sheet are included herewith with the Examiner's convenience.

Oath/Declaration

A new oath or declaration in compliance with 37 C.F.R. §1.67(a) is required. The Examiner noted that the oath is defective because the transmittal, while identifying the instant application as a continuing application, fails to lay claim to prior application number 09/127,620. However, the oath as filed is in full compliance with 37 C.F.R. §1.67(a). The transmittal filed on February 15, 2001 contains information that was later found to be incorrect. The transmittal states that the application is a continuation-in-part of prior application number 08/843,157, which is a continuation-in-part of prior application number 08/581,351. However, as the Examiner has noted, the application as filed stated that the application was a continuation-in-part of application serial number 09/127,620. However, the present application actually claims priority to provisional patent application serial number 60/182,608, filed on February 15, 2000. The application has been amended to correct the priority claim. Accordingly, the oath, which

identifies provisional patent application serial number 60/182,608 as the priority document is in compliance with 37 C.F.R. §1.67(a), and a new oath is not enclosed.

35 U.S.C. §112, First Paragraph

Claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 69, 70, 74, 75, 78, 79 and 83 are rejected under 35 U.S.C.§112, first paragraph, as based on a disclosure that is not enabling and as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants traverse the rejection.

Claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 65, 69, 70, 74, 75, 78, 79 and 83 are fully enabled by the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner argues that that the sixteen amino acids that could be combined to form the peptide of the invention are not listed or defined by the claims. The Examiner also argues that the terminology is not enabled because a plethora of peptides would have to be screened to see which ones would work for the purposes stated in the present invention. However, the U.S. Patent and Trademark Office has no concern over breadth of terms. Recitation of generic terms must be taken as an assertion by the Applicant that all of the peptides that are included within the generic term, "a peptide of sixteen amino acids," would, as a class, be operative to produce the asserted pharmacological benefits. The first paragraph of §112 requires nothing more than objective enablement. The specification disclosure that contains the teaching of the matter and process of making an using the invention in terms of the corresponding scope to those used in describing the claimed invention must be taken as in compliance with the enabling requirement of the first paragraph of §112, unless there is a reason

to doubt the truth of the statements contained therein that must be relied on for enabling support. *In re Marzocchi & Horton*, 169 USPQ 367 (CCPA 1971). The Examiner's attention is directed to the specification, page 17, lines 16-20, where picolinic acid having substitutions made with a peptide of sixteen amino acids at the 3, 4, 5 or 6 position is described. As discussed in the specification, the specific amino acids employed in the peptide of the invention are not critical so long as the substituted picolinic acid has an increased molecular weight and a substantial increased half-life in the blood as a result of the substitution. No amino acids would need to be screened to see which ones would work so long as sixteen of them are combined to form the peptide. The only critical feature of the peptide is that it comprises sixteen amino acids, which is both claimed and described in the specification. Therefore, it is requested that the rejection of claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 69, 70, 74, 75, 78, 79 and 83 under 35 U.S.C.§112, first paragraph, be withdrawn.

Claims 13, 18, 21 and 39 are rejected under 35 U.S.C. §112, first paragraph. The Examiner argues that the specification, while enabling for treating certain viruses, does not reasonably provide enablement for the treatment of all diseases associated with decreased immune function.

Claims 13, 18, 21 and 39 have been amended to remove "decreased immune function" as a condition that is treated by the administration of the compounds of the invention. Accordingly, it is submitted that claims 13, 18, 21 and 39, as amended, are fully enabled. Therefore, it is respectfully requested that the rejection of claims 13, 18, 21 and 39 under 35 U.S.C. §112, first paragraph, be withdrawn.

35 U.S.C. §112, Second Paragraph

Claims 13-47 and 59-83 are rejected under 3 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Specifically, the Examiner argues that it is unclear whether the Applicant is intending to encompass a composition or method claim in claims 13-20, 59-64, 21-42, 65-69 and 43-47. In addition, the Examiner argues that acceptable routes of administration are not described in claims 43-47. With regard to claims 70 and 74, the Examiner argues that that the phrase "a lavage comprising up to about 99%" is indefinite and vague because it reads on 0%. With regard to claims 75 and 78, the Examiner argues that the phrase "preservative comprising less than about 0.025%..." is vague and indefinite for the same reasons. With regard to claims 79, 81 and 83, the Examiner argues that employing the word "contacting" renders the claims indefinite, as it is unclear if the two ingredients are physically contacted with each other, or if they are reacted together thus causing a chemical reaction. With regard to claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 69, 70, 74, 75, 78, 79 and 83, the Examiner argues that the phrase "a peptide of sixteen amino acids" was inoperative and rendered the claims indefinite.

With regard to the Examiner's argument that it is unclear whether Applicant is intending to encompass a composition or method in claims 13-20, 21-42, 43-47, 59-64, and 65-69, Applicant submits that the claims, as amended, clearly state whether they are method or composition claims. Claims 13 and 18, as amended, are clearly composition claims. The claims read, "A pharmacologically active metal ion chelating agent adapted for the treatment of a disease... the agent having the following structure..." Claims 13 and 18 do not include a single method or process step, and therefore cannot be method or process claims.

Claims 14-17 and 19-20, which depend from amended claims 13 and 18, respectively, are also clearly composition claims. They refer to "The metal ion chelating agent of claim ..." Claims 14-17 and 19-20 do not include a single method or process step, and therefore cannot be method or process claims.

Claims 21 and 39, as amended, are clearly method claims. The Examiner states that the claims read, " a method for the treatment of ... comprising a ... chelating agent..." in line 1. However, the Examiner misreads the claims. The claims read, "A method comprising administering an effective amount of a pharmaceutical composition..." The preamble of the claims state that they are method claims and the step of administering an effective amount of the pharmaceutical composition is present in both claims. Accordingly, it is clear that amended claims 21 and 39 are method claims.

Claims 22-38 and 40-42 are also clearly method claims. Since claims 22-38 and 40-42 depend from amended claims 21 and 39, respectively, they must too be method claims. In addition, claims 22-38 and 40-42 all state in their preambles that the claims are directed to a "method."

Claims 43, as amended, and 47 are clearly composition claims. The claims read, "A systemic preparation comprising..." No method or process step is recited in either claim. Therefore the claims cannot be method or process claims, and it is requested that the rejection of claim 43, as amended, and claim 47 under 35 U.S.C. §112, second paragraph, be withdrawn.

Dependent claims 44-46 are also clearly composition claims. Since claims 44-46 depend from amended claim 43, they must too be composition claims. In addition, claims 44-46 all state in their preambles that the claims are directed to a "systemic preparation." Therefore, the claims

cannot be method or process claims, and it is requested that the rejection of claims 44-46 under 35 U.S.C. §112, second paragraph, be withdrawn.

With regard to the Examiner's argument that acceptable routes of administration are not described in claims 43-47, Applicant traverses the rejection. Claim 43, as amended, is directed to a systemic preparation that comprises a metal ion chelating agent and a pharmacologically acceptable carrier. The requirements of the second paragraph of §112 are met when the specification is in compliance with the first paragraph of §112, and the claims are commensurate in scope with the specification. *In re Borkowski and Van Venroy*, 164 USPQ 642 (CCPA 1970). If the scope of the subject matter embraced by a claim is clear and if the Applicant has not otherwise indicated that he intends the claim to be of a different scope, then the claim particularly points out and distinctly claims the subject matter which the Applicant regards as the invention. *Id.* Breadth alone is not indefiniteness. *In re Gardner et al.*, 427 F.2d 786 (CCPA 1970). Therefore, it is respectfully requested that the rejection of claims 43, as amended, and claim 47 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claim 59, as amended, and claim 63, as amended, are clearly directed to formulations, and not method claims. The claims read, "A formulation adapted for the treatment of ... comprising..." There is no method or process step recited. Therefore, the claims cannot be method claims. Therefore, it is respectfully requested that the rejection of claims 59 and 63, as amended, under 35 U.S.C. §112, second paragraph, be withdrawn.

Claims 60-62 and 64 are also clearly not method claims. Since claims 60-62 and 64 depend from claims 59, as amended, and 63 respectively, they must too be formulation claims. In addition, all of the claims state in their preambles that they are directed to a "formulation."

Therefore, it is respectfully requested that the rejection of claims 60-62 and 64 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claims 65 and 69, as amended, are clearly directed to preparations, and are not method claims. The claims read, "An ophthalmic preparation adapted for the control of angiogenesis comprising..." There is no method or process step recited. Therefore, claims 65 and 69 cannot be interpreted as method claims. Therefore, it is respectfully requested that the rejection of claims 65 and 69 under 35 U.S.C. §112, second paragraph, be withdrawn.

Claims 66-68 are also clearly directed to preparations, and are not method claims. Since claims 66-68 depend from amended claim 65, they must too be formulation claims. In addition, all of the claims state in their preambles that they are directed to an "ophthalmic preparation." Therefore, it is respectfully requested that the rejection of claims 66-68 under 35 U.S.C. §112, second paragraph, be withdrawn.

With regard to claims 70 and 74, the Examiner argued that that the phrase "a lavage comprising up to about 99%" is indefinite and vague because it reads on 0%. Claims 70 and 74 have been amended to remove the limitation. As such, the amended claims do not encompass lavages that are devoid of the claimed metal ion chelating agent. Therefore, it is respectfully requested that the rejection of claims 70 and 74, as amended, under 35 U.S.C. §112, second paragraph, be withdrawn.

With regard to claims 75 and 78, the Examiner argued that the phrase "preservative comprising less than about 0.025%..." was vague and indefinite for the same reasons. Claims 75 and 78 have been amended to remove the limitation. As such, the claims, as amended, clearly does not encompass preservatives that are void of the claimed metal ion chelating agent.

Therefore, it is respectfully requested that the rejection of claims 75 and 78, as amended, under 35 U.S.C. §112, first paragraph, be withdrawn.

The Examiner argued that claims 79, 81 and 83 are indefinite because the term "contacting" is unclear. Specifically, the Examiner argues that it is unclear whether the two ingredients are physically contacted with each other or if they are reacted together thus causing a chemical reaction. Applicants traverse the rejection.

Claims 79, 81 and 83, as amended, are clearly definite. During "patent examination, the pending claims must be 'given the broadest reasonable interpretation consistent with the specification.'" MPEP 2111; *In re Prater*, 415 F.2d 1393, 1404 (CCPA 1969). Further, the "words of the claim must be given their plain meaning unless the applicant has provided a clear definition in the specification." MPEP 2111.01; *In re Zletz*, 893 F.2d 319, 321 Fed. Cir. 1989). Accordingly, the Examiner must interpret the term "contacting" according to its plain meaning, and interpret claims 79, 81 and 83, as amended, in their broadest sense. Therefore, it is respectfully requested that the Examiner withdraw the rejection of claims 79, 81 and 83, as amended, under 35 U.S.C. §112, second paragraph.

Claims 71-73, 76, 77, 80 and 82 have been rejected as being dependent on rejected base claims. Claims 71-73, 76, 77, 80 and 82 depend directly or indirectly from claims 70, 75 and 79, respectively. Since it is submitted for the reasons stated herein that claims 70, 75 and 79 are patentable, it is also submitted that claims 71-73, 76, 77, 80 and 82 are likewise patentable for the same reasons. Accordingly, Applicant requests withdrawal of the rejection of 71-73, 76, 77, 80 and 82 under 35 U.S.C. §112, second paragraph.

Claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 65, 69, 70, 74, 75, 78, 79 and 83 were rejected as being indefinite because they contain the phrase "a peptide of sixteen amino acids," which the Examiner argues is inoperative. Applicants traverse the rejection.

Claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 65, 69, 70, 74, 75, 78, 79 and 83 particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner argues that one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention because the sixteen amino acids that could be combined to form the peptide are not listed or defined by the claims. However, the requirements of the second paragraph of §112 are met when the specification is in compliance with the first paragraph of §112, and the claims are commensurate in scope with the specification. *In re Borkowski and Van Venroy*, 164 USPQ at 642. The first sentence of the second paragraph of §112 is essentially a requirement for precision and definiteness of claim language. If the scope of the subject matter embraced by the claim is clear, and if the Applicant has not otherwise indicated that he intends the claim to be of a different scope, then the claim particularly points out and distinctly claims the subject matter which the Applicant regards as the invention. *In re Borkowski and Van Venroy*, 164 USPQ at 642. Therefore, it is requested that the rejection of claims 13, 18, 21, 39, 43, 47, 48, 53, 54, 58, 59, 63, 69, 70, 74, 75, 78, 79 and 83 under 35 U.S.C.§112, second paragraph, be withdrawn.

35 U.S.C. § 102(b)

Claims 13-22, 24, 28-30, 32-34, 38-40 and 43-74 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,582,817 to Otsu et al. Applicant traverses the rejection.

Otsu et al. describes a method of suppressing the production of sunburn cells, a method of inducing metallothionein, a method of treating skin diseases and a method of screening UV

rays by the administration of an effective amount of zinc picolinate. Column 3, lines 1-22. Otsu et al. does not mention or suggest the use of picolinic acid or fusaric acid for the treatment of hepatitis C infections, angiogenesis, metastatic colon cancer or upper respiratory infections. Further, Otsu et al. does not mention or suggest treatment of sunburn by the administration of picolinic acid, or derivatives thereof that is not zinc picolinate.

Claim 13, as amended, is directed to pharmacologically active picolinic acid, fusaric acid, pharmacologically acceptable salt or derivatives thereof adapted for the treatment of hepatitis C infections, angiogenesis, sunburn, metastatic colon cancer and upper respiratory infections, wherein when the picolinic acid, fusaric acid, or a pharmacologically acceptable salt or derivative thereof is adapted for the treatment of sunburn, the agent is not zinc picolinate.

Claim 13 is not anticipated by Otsu et al. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628 (Fed. Cir. 1987). Otsu et al. does not describe picolinic acid, fusaric acid, or a pharmacologically acceptable salt or derivatives thereof adapted for the treatment of hepatitis C infections, angiogenesis, sunburn, metastatic colon cancer or upper respiratory infections, wherein when the agent is adapted for the treatment of sunburn, the agent is not zinc picolinate. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. Otsu et al. does not describe the use of zinc picolinate adapted for the treatment of hepatitis C infections, angiogenesis, metastatic colon caner or upper respiratory infections. These conditions are not discussed in Otsu et al. Claim 13, as amended, is not directed to and does not encompass zinc picolinate adapted for the treatment of sunburn. Accordingly, amended

claim 13 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of amended claim 13 under 35 U.S.C. §102(b) be withdrawn.

Claims 14-17 depend from amended claim 13, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 13 is patentable over Otsu et al., it is likewise submitted that claims 14-17 are patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claims 14-17 under 35 U.S.C. §102(b) be withdrawn.

Claim 18, as amended, is not anticipated by Otsu et al. Otsu et al. does not describe fusaric acid adapted for the treatment of hepatitis C infections, angiogenesis, sunburn, metastatic colon cancer and upper respiratory infections, wherein the disease, disorder or condition is mediated by a protein having a metal ion-protein complex. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of a zinc picolinate. No where in Otsu et al. is the use of fusaric acid discussed. Claim 18, as amended, is not directed to and does not encompass zinc picolinate, or picolinic acid. Accordingly, amended claim 18 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of amended claim 18 under 35 U.S.C. §102(b) be withdrawn.

Claims 19 and 20 depend from amended claim 18, and therefore incorporate all of the limitations therein. Since it is submitted for the aforementioned reasons that claim 18 is patentable over Otsu et al., it is likewise submitted that claims 19 and 20 are patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claims 19 and 20 under 35 U.S.C. §102(b) be withdrawn.

Claim 21, as amended, is directed to a method comprising administering an effective amount of picolinic acid, fusaric acid, pharmacologically acceptable salts or derivatives thereof to an individual having metastatic colon cancer, hepatitis C infections, angiogenesis, sun burn, or upper respiratory infections, wherein when said method is for the treatment of sunburn the agent is not zinc picolinate. Otsu et al. does not describe methods of treating hepatitis C infections, angiogenesis, metastatic colon cancer and upper respiratory infections by the administration of picolinic acid, fusaric acid, pharmacologically acceptable salts or derivatives thereof. Further, Otsu et al. does not describe methods of treating sunburn by the administration of pharmacologically acceptable salts of picolinic acid other than zinc picolinate. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid or picolinic acid to treat metastatic colon cancer, hepatitis C infections, angiogenesis, sun burn, or upper respiratory infections discussed. Claim 21, as amended, is not directed to and does not encompass methods of treating sunburn by the administration of zinc picolinate. Accordingly, amended claim 21 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 21 under 35 U.S.C. §102(b) be withdrawn.

Claims 22-38 depend either directly or indirectly from amended claim 21, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 21 is patentable over Otsu et al., it is likewise submitted that claims 22-38 are patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claims 22, 24, 28-30, 32-34 and 38 under 35 U.S.C. §102(b) be withdrawn.

Claim 39, as amended, is directed to a method comprising administering an effective amount of fusaric acid or pharmacologically acceptable salts or derivatives thereof to an individual having metastatic colon cancer, hepatitis C infections, angiogenesis, sun burn, inflammation associated with acne, or an upper respiratory infection. Otsu et al. does not describe methods for the treatment of hepatitis C infections, angiogenesis, sunburn, the inflammation associated with acne, metastatic colon cancer or upper respiratory infections by the administration of fusaric acid. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid to treat metastatic colon cancer, hepatitis C infections, the inflammation associated with acne, angiogenesis, sun burn, or upper respiratory infections discussed. Claim 39, as amended, is not directed to and does not encompass methods treating sunburn by the administration of zinc picolinate. Accordingly, amended claim 39 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 39 under 35 U.S.C. §102(b) be withdrawn.

Claims 40-42 depend from amended claim 39, and therefore incorporate all of the limitations therein. Since it is submitted for the aforementioned reasons that amended claim 39 is patentable over Otsu et al., it is likewise submitted that claims 40-42 are patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claim 40 under 35 U.S.C. §102(b) be withdrawn.

Claim 43, as amended, is directed to a systemic preparation comprising approximately 1% to approximately 100% fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof and a pharmacologically acceptable carrier, wherein the preparation does not

comprise zinc picolinate. Otsu et al. does not describe systemic preparations comprising fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof, other than zinc picolinate. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof, other than zinc picolinate, in a systemic preparation described. Claim 43, as amended, is not directed to a systemic preparation comprising zinc picolinate. Accordingly, amended claim 43 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 43 under 35 U.S.C. §102(b) be withdrawn.

Claims 44-46 depend from amended claim 43, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 43 is patentable over Otsu et al., it is likewise submitted that claims 44-46 are patentable over Otsu et al. Therefore, it is respectfully requested that the rejection of claims 44-46 under 35 U.S.C. §102(b) be withdrawn.

Claim 47 is directed to a systemic preparation comprising approximately 1% to approximately 100% fusaric acid or a pharmacologically acceptable salt or derivative thereof and a pharmacologically acceptable route of administration. Otsu et al. does not describe systemic preparations comprising approximately 1% to approximately 100% fusaric acid or a pharmacologically acceptable salt or derivative thereof. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid in a systemic preparation described. Claim 47, as amended,

is not directed to a systemic preparation comprising zinc picolinate. Accordingly, amended claim 47 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 47 under 35 U.S.C. §102(b) be withdrawn.

Claim 48, as amended, is directed to an intranasal solution comprising about 0.01mM to about 50mM fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof and at least one nebulizing agent, wherein the intranasal solution does not comprise zinc picolinate. Otsu et al. does not describe intranasal solutions comprising fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof, other than zinc picolinate. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of a zinc picolinate. No where in Otsu et al. is the use of fusaric acid or picolinic acid in an intranasal solution described. Claim 48, as amended, is not directed to an intranasal solution comprising zinc picolinate. Accordingly, amended claim 48 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 48 under 35 U.S.C. §102(b) be withdrawn.

Claims 49-52 depend from amended claim 48, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 48 is patentable over Otsu et al., it is likewise submitted that claims 49-52 are patentable over Otsu et al. Therefore, it is respectfully requested that the rejection of claims 49-52 under 35 U.S.C. §102(b) be withdrawn.

Claim 53 is directed to an intranasal solution comprising about 0.01mM to about 50mM fusaric acid or a pharmacologically acceptable salt thereof and at least one nebulizing agent. Otsu et al. does not describe intranasal solutions comprising fusaric acid or a pharmacologically

acceptable salt thereof. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of a zinc picolinate. No where in Otsu et al. is the use of fusaric acid, or a pharmacologically acceptable salt thereof, in an intranasal solution described. Claim 53 is not directed to an intranasal solution comprising zinc picolinate. Accordingly, claim 53 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 53 under 35 U.S.C. §102(b) be withdrawn.

Claim 54 is directed to an inhalant comprising about 0.001% to about 50% fusaric acid, picolinic acid or a pharmacologically acceptable salt or derivative thereof and at least one nebulizing agent. Otsu et al. does not describe inhalants comprising about 0.001% to about 50% fusaric acid, picolinic acid or a pharmacologically acceptable salt or derivative thereof. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof, in an inhalant described. Claim 54 is not directed to an inhalant comprising zinc picolinate. Accordingly, claim 54 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 54 under 35 U.S.C. §102(b) be withdrawn.

Claims 55-57 depend from claim 54, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that claim 54 is patentable over Otsu et al., it is likewise submitted that claims 55-57 are patentable over Otsu et al. Therefore, it is respectfully requested that the rejection of claims 55-57 under 35 U.S.C. §102(b) be withdrawn.

Claim 58 is directed to an inhalant comprising about 0.001% to about 50% fusaric acid, or a pharmacologically acceptable salt or derivative thereof, and at least one nebulizing agent. Otsu et al. does not describe inhalants comprising about 0.001% to about 50% fusaric acid, or a pharmacologically acceptable salt or derivative thereof. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of a zinc picolinate. No where in Otsu et al. is the use of fusaric acid, or a pharmacologically acceptable salt or derivative thereof, in an inhalant described. Claim 58 is not directed to an inhalant comprising zinc picolinate. Accordingly, claim 58 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of claim 58 under 35 U.S.C. §102(b) be withdrawn.

Claim 59, as amended, is directed to a formulation adapted for the treatment of sunburn comprising about 1% to about 99% fusaric acid, picolinic acid or a pharmacologically acceptable salt or derivative thereof and a topical lotion, wherein the formulation does not comprise zinc picolinate. Otsu et al. does not describe formulations adapted for the treatment of sunburn comprising about 1% to about 99% fusaric acid, picolinic acid, or a pharmacologically acceptable salt or derivative thereof and a topical lotion, wherein the formulation does not comprise zinc picolinate. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of pharmacologically acceptable salts of picolinic acid, other than zinc picolinate, adapted for the treatment of sunburn described. Claim 59, as amended, is not directed to a formulation comprising zinc picolinate. Accordingly, amended claim 59 is not anticipated by Otsu et al.

Therefore, it is respectfully requested that the rejection of claim 59 under 35 U.S.C. §102(b) be withdrawn.

Claims 60-62 depend from amended claim 59, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 59 is patentable over Otsu et al., it is likewise submitted that claims 60-62 are patentable over Otsu et al. Therefore, it is respectfully requested that the rejection of claims 60-62 under 35 U.S.C. §102(b) be withdrawn.

Claim 63, as amended, is directed to a formulation adapted for the treatment of inflammation associated with acne and sunburn comprising from about 1% to about 99% fusaric acid and a topical lotion. Otsu et al. does not describe formulations adapted for the treatment of inflammation associated with acne or sunburn comprising about 1% to about 99% fusaric acid. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid described. Claim 63, as amended, is not directed to a formulation comprising a zinc complex. Accordingly, amended claim 63 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of amended claim 63 under 35 U.S.C. §102(b) be withdrawn.

Claim 64 depends from amended claim 63, and therefore incorporates all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 63 is patentable over Otsu et al., it is likewise submitted that claim 64 is patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claim 64 under 35 U.S.C.§102(b) be withdrawn.

Claim 65, as amended, is directed to an ophthalmic preparation for the control of angiogenesis comprising about 0.01% to about 99% fusaric acid, picolinic acid, or a pharmacologically acceptable salt thereof, and a pharmacologically acceptable carrier. Otsu et al. does not describe ophthalmic preparations comprising about 0.01% to about 99% fusaric acid, picolinic acid, or a pharmacologically acceptable salt thereof, and a pharmacologically acceptable carrier. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid, picolinic acid, or a salt thereof, in an ophthalmic preparation described. Accordingly, amended claim 65 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of amended claim 65 under 35 U.S.C. §102(b) be withdrawn.

Claims 66-68 depend from amended claim 65, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 65 is patentable over Otsu et al., it is likewise submitted that claims 66-68 are patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claims 66-68 under 35 U.S.C. §102(b) be withdrawn.

Claim 70, as amended, is directed to a lavage comprising fusaric acid, picolinic acid, or a pharmacologically acceptable salt thereof. Otsu et al. does not describe lavages comprising fusaric acid, picolinic acid, or a salt thereof. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. are lavages described. Accordingly, amended claim 70 is not anticipated by Otsu et al.

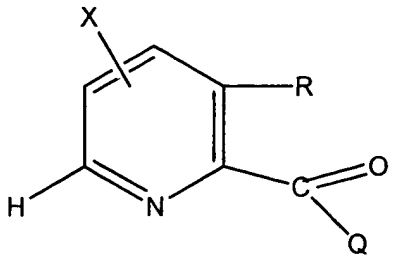
Therefore, it is respectfully requested that the rejection of amended claim 70 under 35 U.S.C. §102(b) be withdrawn.

Claims 71-73 depend from amended claim 70, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 70 is patentable over Otsu et al., it is likewise submitted that claims 71-73 are patentable over Otsu et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claims 71-73 under 35 U.S.C. §102(b) be withdrawn.

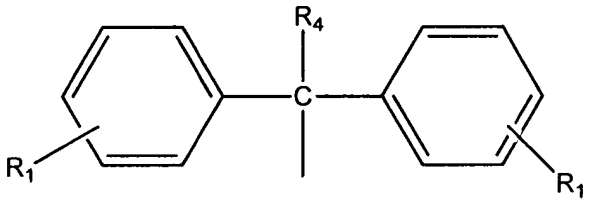
Claim 74, as amended, is directed to a lavage comprising fusaric acid, or a pharmacologically acceptable salt thereof. Otsu et al. does not describe lavages comprising fusaric acid. Rather, Otsu et al. describes methods of suppressing the production of sunburn cells, inducing metallothionein, treating skin diseases and screening UV rays by the administration of an effective amount of zinc picolinate. No where in Otsu et al. is the use of fusaric acid, or salts thereof, described. Accordingly, amended claim 74 is not anticipated by Otsu et al. Therefore, it is respectfully requested that the rejection of amended claim 74 under 35 U.S.C. §102(b) be withdrawn.

Claims 18, 20 and 39-43 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 4,138,488 to Sherlock et al. Applicants respectfully traverse the rejection.

Sherlock et al. discloses picolinic acids and fusaric acids bearing diphenylmethyl or substituted diphenylmethyl substituents adapted for the treatment of acne. Column 1, lines 10-50. The substituted picolinic acids described are represented by the following structural formula:

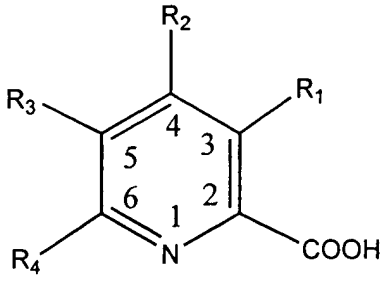


and the pharmaceutically acceptable salts thereof, wherein X is a diphenylmethyl group represented by the following structure:



Column 1, lines 10-50.

Claim 18, as amended, is not anticipated by Sherlock et al. Claim 18 is directed to a pharmacologically active metal ion chelating agent adapted for the treatment hepatitis C infections, angiogenesis, sun burn, inflammation associated with acne, metastatic colon cancer and upper respiratory infections, wherein the disease, disorder or condition is mediated by a protein having a metal ion-protein complex, the agent having the following structure:



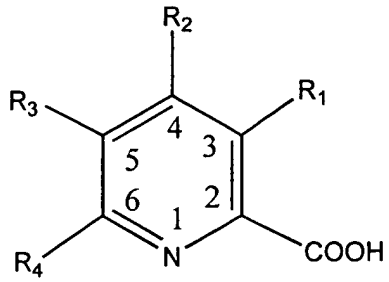
or a pharmacologically acceptable salt thereof,

wherein R_1, R_2, or R_4 are independently selected from the group consisting of a peptide of sixteen amino acids, carboxyl group, methyl group, ethyl group, propyl group, isopropyl

group, butyl group, isobutyl group, secondary butyl group, tertiary butyl group, pentyl group, isopentyl group, neopentyl group, fluorine, chlorine, bromine, iodine, and hydrogen; and R_3 is a butyl group. Sherlock does not describe fusaric acid substituted at the R_1, R_2, R_3 or R_4 positions with lower alkyl groups and/or peptides consisting of amino acids. Rather, Sherlock et al. describes fusaric acids that are substituted with a diphenylmethyl group at the R_2 or R_3 position. Further, Sherlock et al. does not describe the use of any substituted fusaric acid adapted for the treatment hepatitis C infections, angiogenesis, sun burn, metastatic colon cancer or upper respiratory infections. Accordingly, amended claim 18 is not anticipated by Sherlock et al. Therefore, it is respectfully requested that the rejection of amended claim 18 under 35 U.S.C. §102(b) be withdrawn.

Claims 19-20 depend from amended claim 18, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that amended claim 18 is patentable over Sherlock et al., it is likewise submitted that claims 19-20 are patentable over Sherlock et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claim 20 under 35 U.S.C. §102(b) be withdrawn.

Claim 39 is directed to a method comprising administering an effective amount of a pharmaceutical composition comprising a metal ion chelating agent to an individual having metastatic colon cancer, hepatitis C infections, angiogenesis, sun burn, inflammation associated with acne or an upper respiratory infection, the metal ion chelating agent represented by the following structure:

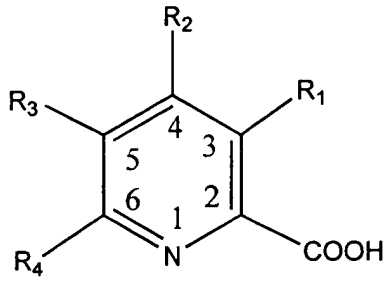


or a pharmacologically acceptable salt thereof,

wherein R_1, R_2, or R_4 are independently selected from the group consisting of a peptide of sixteen amino acids, carboxyl group, methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, secondary butyl group, tertiary butyl group, pentyl group, isopentyl group, neopentyl group, fluorine, chlorine, bromine, iodine and hydrogen; and R_3 is a butyl group. Sherlock does not describe a method of treating metastatic colon cancer, hepatitis C infections, angiogenesis, sun burn, inflammation associated with acne or upper respiratory infection by the administration of fusaric acid substituted at the R_1, R_2, R_3 or R_4 positions with lower alkyl groups and/or peptides consisting of amino acids. Rather, Sherlock et al. describes fusaric acids that are substituted with a diphenylmethyl group at the R_2 or R_3 position. Further, Sherlock et al. does not describe the use of any substituted fusaric acid for the treatment hepatitis C infections, angiogenesis, sun burn, metastatic colon cancer or upper respiratory infections. Accordingly, amended claim 39 is not anticipated by Sherlock et al. Therefore, it is respectfully requested that the rejection of amended claim 39 under 35 U.S.C. §102(b) be withdrawn.

Claims 40-42 depend from independent claim 39, and therefore incorporate all of the subject matter therein. Since it is submitted for the aforementioned reasons that independent claim 39 is patentable over Sherlock et al., it is likewise submitted that claims 40-42 are patentable over Sherlock et al. for the same reasons. Therefore, it is respectfully requested that the rejection of claims 40-42 under 35 U.S.C. §102(b) be withdrawn.

Claim 43, as amended, is directed to a systemic preparation comprising approximately 1mM to approximately 100mM metal ion chelating agent and a pharmacologically acceptable route of administration, wherein said metal ion chelating agent is represented by the following structure:



or a pharmacologically acceptable salt thereof,

wherein R_1, R_2, R_3 or R_4 are independently selected from the group consisting of a peptide of sixteen amino acids, carboxyl group, methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, secondary butyl group, tertiary butyl group, pentyl group, isopentyl group, neopentyl group, fluorine, chlorine, bromine, iodine, and hydrogen. Sherlock does not describe a systemic preparation comprising picolinic acid substituted at the R_1, R_2, R_3 or R_4 positions with lower alkyl groups and/or peptides consisting of amino acids. Rather, Sherlock et al. describes picolinic acids that are substituted with a diphenylmethyl group at the R_2 or R_3 positions. Further, Sherlock et al. does not describe the use of any substituted picolinic acid for the treatment hepatitis C infections, angiogenesis, sun burn, metastatic colon cancer or upper respiratory infections. Accordingly, amended claim 43 is not anticipated by Sherlock et al. Therefore, it is respectfully requested that the rejection of amended claim 43 under 35 U.S.C. §102(b) be withdrawn.

Applicant respectfully submits that the amendments herein place the application in condition for allowance. If the amended patent application is not in condition for allowance, it is

requested that Examiner contact Applicant's undersigned attorney by telephone. Applicant's undersigned attorney may be reached in St. Louis, MO, USA by telephone at (314) 552-6123 or by facsimile at (314) 552-7123. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

Thompson Coburn LLP

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REPLACEMENT PARAGRAPH SHEET

U.S. PATENT APPLICATION NO. 09/784,631

This application claims priority under 35 U.S.C. §119(e) to provisional patent application serial number 60/182,608, filed February 15, 2000.